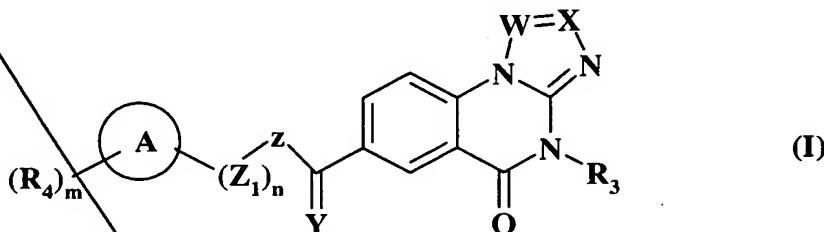


Claims

1 – A compound selected from those of formula (I):

The invention relates to cyclized quinazolines of formula (I)



5 in which:

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W represents N or C-R₁; in which R₁ is selected from:

- hydrogen atom,
- OR₅, SR₅ in which R₅ is selected from hydrogen, (C₁-C₆)alkyl and aryl(C₁-C₆)alkyl,
- (C₁-C₆)alkyl, cycloalkyl of 3 to 8 carbon atoms optionally interrupted with one hetero atom selected from oxygen, sulfur and nitrogen, aryl, heteroaryl and aryl(C₁-C₆)alkyl, these groups being optionally substituted by (CH₂)_p-OH or (CH₂)_p-NH₂, in which p is an integer from 0 to 4 inclusive,

X represents N or C-R₂ in which R₂ is selected from:

- hydrogen atom,
- NR₆R₇, OR₆, SR₆ in which R₆ and R₇, identical or different, are selected from hydrogen, (C₁-C₆)alkyl and aryl(C₁-C₆)alkyl,
- (C₁-C₆)alkyl, cycloalkyl of 3 to 8 carbon atoms optionally interrupted with one hetero atom selected from oxygen, sulfur and nitrogen, aryl, heteroaryl and aryl(C₁-C₆)alkyl, these groups being optionally substituted by (CH₂)_p-OH or (CH₂)_p-NH₂, in which p is an integer from 0 to 4 inclusive,

Y represents a group selected from oxygen, sulfur, -NH, and -N(C₁-C₆)alkyl,

Z represents a group selected from:

- oxygen, sulphur,
- and -NR₈ in which R₈ represents a group selected from hydrogen, (C₁-C₆)alkyl, aryl(C₁-C₆)alkyl, cycloalkyl, aryl, and heteroaryl, and
- when Y is oxygen, sulphur, or -N(C₁-C₆)alkyl, Z optionally represents a carbon atom which is optionally substituted by a group selected from (C₁-C₆)alkyl, aryl, aryl(C₁-C₆)alkyl, aromatic heterocycle, non-aromatic heterocycle, and cycloalkyl,

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n is an integer from 0 to 8 inclusive,

Z₁ represents a group -CR₉R₁₀ wherein R₉ and R₁₀, identical or different, represent a group selected from hydrogen, (C₁-C₆)alkyl, halo(C₁-C₆)alkyl, halogen, NR₅R₁₁, OR₅, SR₅ and C(=O)OR₅ in which R₅ and R₁₁, identical or different, represents hydrogen atom or (C₁-C₆)alkyl, and

- when n is greater than or equal to 2, the hydrocarbon chain Z₁ optionally contains one or more multiple bonds,
- and/or one of the carbon atoms in the hydrocarbon chain Z₁ may be replaced with an oxygen atom, a sulphur atom which is optionally substituted by one or two oxygen atoms, or a nitrogen atom which is optionally substituted by (C₁-C₆)alkyl,

A represents a group selected from :

- aromatic or non-aromatic, 5- or 6-membered monocycle comprising from 0 to 4 heteroatoms selected from nitrogen, oxygen and sulphur, and
- bicycle, composed of two aromatic or non-aromatic, 5- or 6-membered rings, which may be identical or different, comprising from 0 to 4 heteroatoms selected from nitrogen, oxygen and sulphur,

m is an integer from 0 to 7 inclusive,

the group(s) R₄, which may be identical or different, is (are) selected from (C₁-C₆)alkyl, halogen, -CN, -NO₂, -SCF₃, -CF₃, -OCF₃, -NR₅R₁₁, -OR₅, -SR₅, -SOR₅, -SO₂R₅, -(CH₂)_kSO₂NR₅R₁₁, -X₁(CH₂)_kC(=O)OR₅, -(CH₂)_kC(=O)OR₅, -X₁(CH₂)_kC(=O)NR₅R₁₁, -(CH₂)_kC(=O)NR₅R₁₁, and -X₂-R₁₂ in which:

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- 5 • X_1 represents a group selected from oxygen, sulphur optionally substituted by one or two oxygen atoms, and nitrogen substituted by hydrogen or (C_1 - C_6)alkyl,

- k is an integer from 0 to 3 inclusive,

- R_5 and R_{11} , which may be identical or different, are selected from hydrogen and (C_1 - C_6)alkyl,

- 10 • X_2 represents a group selected from single bond, - CH_2 -, oxygen atom, sulphur atom optionally substituted by one or two oxygen atoms, and nitrogen atom substituted by hydrogen atom or (C_1 - C_6)alkyl group,

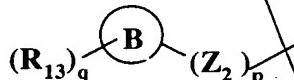
- 15 • R_{12} represents an aromatic or non-aromatic, heterocyclic or non-heterocyclic, 5- or 6-membered ring which is optionally substituted by one or more groups, which may be identical or different, selected from (C_1 - C_6)alkyl, halogen, hydroxyl and amino, and when the ring is heterocyclic, it comprises from 1 to 4 heteroatoms selected from nitrogen, oxygen and sulphur,

R_3 represents a group selected from:

- 20 • hydrogen,

- (C_1 - C_6)alkyl, (C_2 - C_6)alkenyl, (C_2 - C_6)alkynyl, these groups being optionally substituted by one or more groups, which may be identical or different, selected from amino, cyano, halo(C_1 - C_6)alkyl, cycloalkyl, - $C(=O)NR_5R_{11}$, - $C(=O)OR_5$, - OR_5 , and - SR_5 , in which R_5 and R_{11} , which may be identical or different, are as defined hereinbefore,

- and the group of formula :



✓ in which p is an integer from 0 to 8 inclusive,

✓ Z_2 represents - $CR_{14}R_{15}$ wherein R_{14} and R_{15} , identical or different, represent a group selected from hydrogen, (C_1 - C_6)alkyl, phenyl, halo(C_1 - C_6)alkyl, halogen, amino, - OR_5 ,

~~-NR₅R₁₁, -SR₅ and -C(=O)OR₅ in which R₅ and R₁₁, identical or different, are as defined hereinbefore, and~~

- ~~- when p is greater than or equal to 2, the hydrocarbon chain Z₂ optionally contains one or more multiple bonds,~~
- ~~- and/or one of the carbon atoms in the hydrocarbon chain Z₂ may be replaced with an oxygen atom, a sulphur atom which is optionally substituted by one or two oxygen atoms, or a nitrogen atom which is optionally substituted by (C₁-C₆)alkyl,~~

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✓ B represents a group selected from:

- aromatic or non-aromatic 5- or 6-membered monocycle comprising from 0 to 4 heteroatoms selected from nitrogen, oxygen and sulphur, and
- bicyclic, composed of two aromatic or non-aromatic, 5- or 6-membered rings, which may be identical or different, comprising from 0 to 4 heteroatoms selected from nitrogen, oxygen and sulphur,

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ELEMENTS OF
DEFINITION

✓ q is an integer from 0 to 7 inclusive,

15

✓ the group(s) R₁₃, which may be identical or different, is (are) selected from (C₁-C₆)alkyl, halogen, -CN, -NO₂, -CF₃, -OCF₃, (C₁-C₆)acyl, -(CH₂)_kNR₁₆R₁₇, -X₃-(CH₂)_kNR₁₆R₁₇, -N(R₁₆)C(=O)R₁₇, -N(R₁₆)C(=O)OR₁₇, -N(R₁₆)SO₂R₁₇, -N(SO₂R₁₆)₂, -OR₁₆, -S(O)_{k1}R₁₆, -(CH₂)_kSO₂NR₁₆R₁₇, -X₃(CH₂)_kC(=O)OR₁₆, -(CH₂)_kC(=O)NR₁₆R₁₇,

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-C(=O)O-R₁₉-NR₁₆NR₁₇ and-X₄-R₁₈, in which :

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- X₃ represents a group selected from oxygen, sulphur optionally substituted by one or two oxygen atoms, and nitrogen substituted by a hydrogen atom or a (C₁-C₆)alkyl group,
- k is an integer from 0 to 3 inclusive,
- k₁ is an integer from 0 to 2 inclusive,
- R₁₆ and R₁₇, which may be identical or different, are selected from hydrogen and (C₁-C₆)alkyl,

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- X₄ represents a group selected from single bond, -CH₂-, oxygen atom, sulphur atom optionally substituted by one or two oxygen atoms, and nitrogen atom substituted by hydrogen atom or (C₁-C₆)alkyl group,
 - R₁₈ represents an aromatic or non-aromatic, heterocyclic or non-heterocyclic, 5- or 6-membered ring, which is optionally substituted by one or more groups, which may be identical or different, selected from (C₁-C₆)alkyl, halogen, hydroxyl, (C₁-C₆)alkoxy, oxo, cyano, tetrazole, -NR₅R₁₁, and -C(=O)OR₅ wherein R₅ and R₁₁ are as defined hereinbefore, and, when the ring is heterocyclic, it comprises from 1 to 4 heteroatoms selected from nitrogen, oxygen and sulphur,
 - R₁₉ represents a (C₁-C₆)alkylene group, optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof,
- it being understood that:
- aryl represents a monocycle or bicyclic containing from 5 to 10 and preferably 5 to 6 carbon atoms,
 - heteroaryl represents aryl, as defined hereinbefore, in which one to four carbon atoms are replaced by one to four heteroatoms selected from nitrogen, oxygen and sulphur,
 - cycloalkyl represents monocycle or bicyclic containing from 3 to 10 and preferably from 3 to 6 carbon atoms,
 - heterocycle represents heteroaryl as defined above, heteroaryl partially hydrogenated and cycloalkyl as defined above in which one to four carbon atoms are replaced by one to four heteroatoms selected from oxygen, sulphur and nitrogen,
 - aryl(C₁-C₆)alkyl represents a group in which alkyl contains from 1 to 6 and preferably from 1 to 4 carbon atoms and aryl contains from 5 to 10 and preferably 5 or 6 carbon atoms,
 - cycloalkyl(C₁-C₆)alkyl represents a group in which alkyl contains from 1 to 6 and preferably from 1 to 3 carbon atoms and cycloalkyl contains from 3 to 10 carbon atoms.

2- A compound according to claim 1 characterized in that:

- W is C-R₁ and X is N or C-R₂ in which R₁ and R₂, identical or different, are selected from hydrogen and methyl,

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Y is O,

Z represents an oxygen atom or -NH group,

n is an integer from 0 to 4 inclusive,

5 Z₁ represents a group -CR₉R₁₀ wherein R₉ and R₁₀, identical or different, represent a group selected from hydrogen, (C₁-C₆)alkyl, halo(C₁-C₆)alkyl, halogen, -NR₅R₁₁, -OR₅, -SR₅ and -C(=O)OR₅ in which R₅ and R₁₁, identical or different, represent hydrogen atom or (C₁-C₆)alkyl, and

- when n is greater than or equal to 2, the hydrocarbon chain Z₁ optionally contains one double bonds,
- and/or one of the carbon atoms in the hydrocarbon chain Z₁ may be replaced with an oxygen atom, a sulphur atom which is optionally substituted by one or two oxygen atoms, or a nitrogen atom which is optionally substituted by (C₁-C₆)alkyl,

10 R₃, R₄ and A are as defined in the compound of formula (I),
 optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

15 3- A compound according to claim 1 characterized in that:

R₃ represents the group of formula :



- ✓ in which p is an integer from 0 to 4 inclusive,

- 20 ✓ Z₂ represents -CR₁₄R₁₅ wherein R₁₄ and R₁₅, identical or different, represent a group selected from hydrogen and methyl, and when p is greater than or equal to 2, the hydrocarbon chain Z₂ optionally contains one double bond,

✓ B represents a group selected from phenyl, pyridyl, thienyl, imidazolyl, furyl, 1,3-benzodioxolyl, benzodioxinyl, benzothienyl, benzofuryl, 2,1,3-benzothiadiazolyl, benzofurazanyl, and indolyl,

✓ q is an integer from 0 to 7 inclusive,

5 ✓ the group(s) R₁₃, which may be identical or different, is (are) selected from (C₁-C₆)alkyl, halogen, -CN, -CF₃, -NR₁₆R₁₇, -OR₁₆, -(CH₂)_kSO₂NR₁₆R₁₇, -O(CH₂)_kC(=O)OR₁₆, -(CH₂)_kC(=O)OR₁₆, -O(CH₂)_kC(=O)NR₁₆R₁₇, -C(=O)O-R₁₉-NR₁₆R₁₇ and -(CH₂)_kC(=O)NR₁₆R₁₇, in which k is an integer from 0 to 3 inclusive, R₁₆ and R₁₇, which may be identical or different, are selected from hydrogen and (C₁-C₆)alkyl, and R₁₉ represents a (C₁-C₆)alkylene group,

10 W, X, Y, Z, Z₁, n, m, A and R₄ are as defined in the compound of formula (I), optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

15 4- A compound according to claim 1 characterized in that:

n is an integer from 0 to 4 inclusive,

Z₁ represents a group -CR₉R₁₀ wherein R₉ and R₁₀ represent each hydrogen atom, and

- when n is greater than or equal to 2, the hydrocarbon chain Z₁ optionally contains one double bond,
- and/or one of the carbon atoms in the hydrocarbon chain Z₁ may be replaced with an oxygen atom, a sulphur atom which is optionally substituted by one or two oxygen atoms, or a nitrogen atom which is optionally substituted by (C₁-C₆)alkyl,

20 A represents a group selected from phenyl, pyridyl, thienyl, imidazolyl, furyl, 1,3-benzodioxolyl, benzodioxinyl, benzothienyl, benzofuryl, 2,1,3-benzothiadiazolyl, benzofurazanyl, and indolyl,

25 m is an integer from 0 to 7 inclusive,

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the group(s) R₄, which may be identical or different, is (are) selected from (C₁-C₆)alkyl, halogen, -CN, -CF₃, -NR₅R₁₁, -OR₅, and -C(=O)OR₅ in which R₅ and R₁₁, which may be identical or different, are selected from hydrogen and (C₁-C₆)alkyl,

W, X, Y, Z and R₃ are as defined in the compound of formula (I),

5 optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

5- A compound according to claim 1 characterized in that:

W is C-R₁ and X is N or C-R₂ in which R₁ and R₂, identical or different, are selected from hydrogen and methyl,

10 Y is O,

Z represents an oxygen atom or -NH group,

n is an integer from 0 to 4 inclusive,

Z₁ represents a group -CR₉R₁₀ wherein R₉ and R₁₀, identical or different, represent a group selected from hydrogen and methyl, and

- 15 • when n is greater than or equal to 2, the hydrocarbon chain Z₁ optionally contains one or more multiple bonds,
• and/or one of the carbon atoms in the hydrocarbon chain Z₁ may be replaced with an oxygen atom, a sulphur atom which is optionally substituted by one or two oxygen atoms, or a nitrogen atom which is optionally substituted by (C₁-C₆)alkyl,

20 A represents a group selected from phenyl, pyridyl, thienyl, imidazolyl, furyl, 1,3-benzodioxolyl, benzodioxinyl, benzothienyl, benzofuryl, 2,1,3-benzothiadiazolyl, benzofurazanyl, and indolyl,

m is an integer from 0 to 7 inclusive,

the group(s) R_4 , which may be identical or different, is (are) selected from $(C_1-C_6)\text{alkyl}$, halogen, $-\text{CN}$, $-\text{CF}_3$, $-\text{NR}_5R_{11}$, $-\text{OR}_5$, $-\text{SO}_2\text{R}_5$, $-(\text{CH}_2)_k\text{SO}_2\text{NR}_5R_{11}$, $-\text{X}_1(\text{CH}_2)_k\text{C}(=\text{O})\text{OR}_5$, $-(\text{CH}_2)_k\text{C}(=\text{O})\text{OR}_5$, $-\text{X}_1(\text{CH}_2)_k\text{C}(=\text{O})\text{NR}_5R_{11}$, $-(\text{CH}_2)_k\text{C}(=\text{O})\text{NR}_5R_{11}$, and $-\text{X}_2\text{-R}_{12}$ in which:

✓ X_1 represents a group selected from oxygen, sulphur and $-\text{NH}$,

5 ✓ k is an integer from 0 to 3 inclusive,

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10 ✓ R_5 and R_{11} , which may be identical or different, are selected from hydrogen and $(C_1-C_6)\text{alkyl}$,

15 ✓ X_2 represents a group selected from single bond, $-\text{CH}_2-$, oxygen atom, and sulphur atom optionally substituted by one or two oxygen atoms,

✓ R_{12} represents an aromatic or non-aromatic, heterocyclic or non-heterocyclic, 5- or 6-membered ring which is optionally substituted by one or more groups, which may be identical or different, selected from $(C_1-C_6)\text{alkyl}$, halogen, hydroxyl and amino, and when the ring is heterocyclic, it comprises from 1 to 4 heteroatoms selected from nitrogen, oxygen and sulphur;

R_3 represents the group of formula:



✓ in which p is an integer from 0 to 6 inclusive,

20 ✓ Z_2 represents $-\text{CR}_{14}\text{R}_{15}$ wherein R_{14} and R_{15} , identical or different, represent a group selected from hydrogen, $(C_1-C_6)\text{alkyl}$, phenyl, halo(C_1-C_6)alkyl, halogen, amino, OR_5 , SR_5 and $-\text{C}(=\text{O})\text{OR}_5$ in which R_5 is as defined in the compound of formula (I), and

- when p is greater than or equal to 2, the hydrocarbon chain Z_2 optionally contains one or more multiple bonds,

- and/or one of the carbon atoms in the hydrocarbon chain Z_2 may be replaced with an oxygen atom, a sulphur atom which is optionally substituted by one or two oxygen atoms, or a nitrogen atom which is optionally substituted by $(C_1-C_6)alkyl$,

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✓ B represents a group selected from:

- aromatic or non-aromatic 5- or 6-membered monocycle comprising from 0 to 4 heteroatoms selected from nitrogen, oxygen and sulphur, and
- bicyclic, composed of two aromatic or non-aromatic, 5- or 6-membered rings, which may be identical or different, comprising from 0 to 4 heteroatoms selected from nitrogen, oxygen and sulphur,

10

✓ q is an integer from 0 to 7 inclusive,

15

✓ the group(s) R_{13} , which may be identical or different, is (are) selected from $(C_1-C_6)alkyl$, halogen, $-CN$, $-CF_3$, $-NR_{16}R_{17}$, $-OR_{16}$, $-SO_2R_{16}$, $-(CH_2)_kSO_2NR_{16}R_{17}$, $-X_3(CH_2)_kC(=O)OR_{16}$, $-(CH_2)_kC(=O)OR_{16}$, $-X_3(CH_2)_kC(=O)NR_{16}R_{17}$,

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$-(CH_2)_kC(=O)NR_{16}R_{17}$, $-C(=O)O-R_{13}-NR_{16}NR_{17}$ and $-X_4-R_{18}$, in which :

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- X_3 represents a group selected from oxygen atom, sulphur atom and $-NH$ group,
- k is an integer from 0 to 3 inclusive,
- R_{16} and R_{17} , which may be identical or different, are selected from hydrogen and $(C_1-C_6)alkyl$,

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- X_4 represents a group selected from single bond, $-CH_2-$, oxygen atom, and sulphur atom optionally substituted by one or two oxygen atoms,
- R_{18} represents an aromatic or non-aromatic, heterocyclic or non-heterocyclic, 5- or 6-membered ring, which is optionally substituted by one or more groups, which may be identical or different, selected from $(C_1-C_6)alkyl$, halogen, hydroxyl, and amino, and when the ring is heterocyclic, it comprises from 1 to 4 heteroatoms selected from nitrogen, oxygen and sulphur,
- R_{19} represents a $(C_1-C_6)alkylene$ group,

optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

~~6.~~ A compound according to claim 1 characterized in that:

W is C-R₁ and X is N or C-R₂ in which R₁ and R₂, identical or different, are selected from hydrogen and methyl,

Y is O,

5 Z represents an oxygen atom or a -NH group,

n is an integer from 0 to 4 inclusive,

10 Z₁ represents a group -CR₉R₁₀ wherein R₉ and R₁₀, identical or different, represent a group selected from hydrogen and methyl, and

- when n is greater than or equal to 2, the hydrocarbon chain Z₁ optionally contains one double bond,
- and/or one of the carbon atoms in the hydrocarbon chain Z₁ may be replaced with an oxygen atom, a sulphur atom which is optionally substituted by one or two oxygen atoms, or a nitrogen atom which is optionally substituted by (C₁-C₆)alkyl,

15 A represents a group selected from phenyl, pyridyl, thienyl, imidazolyl, furyl, 1,3-benzodioxolyl, benzodioxinyl, benzothienyl, benzofuryl, 2,1,3-benzothiadiazolyl, benzofurazanyl, and indolyl,

m is an integer from 0 to 7 inclusive,

20 the group(s) R₄, which may be identical or different, is (are) selected from (C₁-C₆)alkyl, halogen, -CN, -CF₃, -NR₅R₁₁, -OR₅, and -C(=O)OR₅, in which R₅ and R₁₁, which may be identical or different, are selected from hydrogen and (C₁-C₆)alkyl,

R₃ represents the group of formula:



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- ✓ in which p is an integer from 0 to 4 inclusive,
 - ✓ Z_2 represents $-CR_{14}R_{15}$ wherein R_{14} and R_{15} , identical or different, represent a group selected from hydrogen and methyl, and
 - when p is greater than or equal to 2, the hydrocarbon chain Z_2 optionally contains one double bond,
 - and/or one of the carbon atoms in the hydrocarbon chain Z_2 may be replaced with an oxygen atom, a sulphur atom which is optionally substituted by one or two oxygen atoms, or a nitrogen atom which is optionally substituted by $(C_1-C_6)alkyl$,
 - ✓ B represents a group selected from phenyl, pyridyl, thienyl, imidazolyl, furyl, 1,3-benzodioxolyl, benzodioxinyl, benzothienyl, benzofuryl, 2,1,3-benzothiadiazolyl, benzofurazanyl, and indolyl,
 - ✓ q is an integer from 0 to 7 inclusive,
 - ✓ the group(s) R_{13} , which may be identical or different, is (are) selected from $(C_1-C_6)alkyl$, halogen, $-CN$, $-CF_3$, $-NR_{16}R_{17}$, $-OR_{16}$, $-SO_2R_{16}$, $-(CH_2)_kSO_2NR_{16}R_{17}$, $-X_3(CH_2)_kC(=O)OR_{16}$, $-(CH_2)_kC(=O)OR_{16}$, $-X_3(CH_2)_kC(=O)NR_{16}R_{17}$, $-(CH_2)_kC(=O)NR_{16}R_{17}$, $-C(=O)O-R_{19}-NR_{16}NR_{17}$, and $-X_4-R_{18}$, in which :
 - X_3 represents a group selected from oxygen atom, sulphur atom and -NH group,
 - k is an integer from 0 to 3 inclusive,
 - R_{16} and R_{17} , which may be identical or different, are selected from hydrogen and $(C_1-C_6)alkyl$,
 - X_4 represents a group selected from single bond, $-CH_2-$, oxygen atom, and sulphur atom optionally substituted by one or two oxygen atoms,
 - R_{18} represents an aromatic or non-aromatic, heterocyclic or non-heterocyclic, 5- or 6-membered ring, which is optionally substituted by one or more groups, which may be identical or different, selected from $(C_1-C_6)alkyl$, halogen, hydroxyl, and amino, and when the ring is heterocyclic, it comprises from 1 to 4 heteroatoms selected from nitrogen, oxygen and sulphur,
 - R_{19} represents a $(C_1-C_6)alkylene$ group,

optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

7- A compound according to claim 1 characterized in that:

W is C-R₁ and X is N or C-R₂ in which R₁ and R₂, identical or different, are selected from
5 hydrogen and methyl,

Y is O,

Z represents an oxygen atom or a -NH group,

n is an integer from 0 to 4 inclusive,

Z₁ represents a methylen group, and

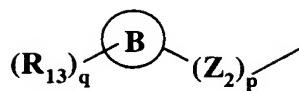
- 10 • when n is greater than or equal to 2, the hydrocarbon chain Z₁ optionally contains one double bond,
• and/or one of the carbon atoms in the hydrocarbon chain Z₁ may be replaced with an oxygen atom, a sulphur atom which is optionally substituted by one or two oxygen atoms, or a nitrogen atom which is optionally substituted by (C₁-C₆)alkyl,

15 A represents a group selected from phenyl, pyridyl, thienyl, imidazolyl, furyl, 1,3-benzodioxolyl, benzodioxinyl, benzothienyl, benzofuryl, 2,1,3-benzothiadiazolyl, benzofurazanyl, and indolyl,

m is an integer from 0 to 7 inclusive,

20 the group(s) R₄, which may be identical or different, is (are) selected from (C₁-C₆)alkyl, halogen, -CN, -CF₃, -NR₅R₁₁, -OR₅, and -C(=O)OR₅, in which R₅ and R₁₁, which may be identical or different, are selected from hydrogen and (C₁-C₆)alkyl,

R₃ represents the group of formula:



- ✓ in which p is an integer from 0 to 4 inclusive,
- ✓ Z_2 represents $-CR_{14}R_{15}$ wherein R_{14} and R_{15} , identical or different, represent a group selected from hydrogen and methyl, and when p is greater than or equal to 2, the hydrocarbon chain Z_2 optionally contains one double bond,
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- ✓ B represents a group selected from phenyl, pyridyl, thienyl, imidazolyl, furyl, 1,3-benzodioxolyl, benzodioxinyl, benzothienyl, benzofuryl, 2,1,3-benzothiadiazolyl, benzofurazanyl, and indolyl,
- ✓ q is an integer from 0 to 7 inclusive,
- 10 ✓ the group(s) R_{13} , which may be identical or different, is (are) selected from (C_1-C_6) alkyl, halogen, $-CN$, $-CF_3$, $-NR_{16}R_{17}$, $-OR_{16}$, $-SO_2R_{16}$, $-(CH_2)_kSO_2NR_{16}R_{17}$, $-O(CH_2)_kC(=O)OR_{16}$, $-(CH_2)_kC(=O)OR_{16}$, $-O(CH_2)_kC(=O)NR_{16}R_{17}$, $-(CH_2)_kC(=O)NR_{16}R_{17}$, and $-C(=O)O-R_{19}-NR_{16}NR_{17}$ in which :
- k is an integer from 0 to 3 inclusive,
 - R_{16} and R_{17} , which may be identical or different, are selected from hydrogen and (C_1-C_6) alkyl,
 - R_{19} represents a (C_1-C_6) alkylene group
- optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.
- 15
- 20 8- A compound according to claim 1 wherein n is equal to one, optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.
- 9- A compound according to claim 1 wherein Z_1 represents a group $-CR_9R_{10}$ in which R_9 and R_{10} represent each a hydrogen atom, optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its the pharmaceutically acceptable salts thereof.

10- A compound according to claim 1 wherein A represents a 5- to 6- membered aromatic monocycle or a 3,4-methylenedioxyphenyl group optionally substituted by one or more groups R₄ as defined in the compound of formula (I), optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

11- A compound according to claim 10 wherein A represents a phenyl group optionally substituted by one group R₄ as defined in the compound of the formula (I), optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

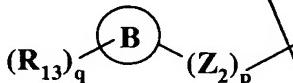
12- A compound according to claim 11 wherein A represents a phenyl group, m is equal to one, and R₄ represents a methoxy group or a fluoro group, optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

13- A compound according to claim 10 wherein A represents a 4-pyridinyl group and m is equal to zero, optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

15 **14** - A compound according to claim 1 wherein Z represents a -NH group and Y represents an oxygen atom, optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

15 - A compound according to claim 1 wherein W represents a -CH group and X represents a nitrogen atom, optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.

16- A compound according to claim 1 wherein R₃ represent a group of formula :



in which p is equal to one, Z₂ represents a methylene group, B represents a phenyl group, q is comprise between 0 to 1 inclusive, R₁₃ represents a group selected from -CN,

~~-(CH₂)_k-C(=O)OR₁₆, -(CH₂)_k-C(=O)NR₁₆R₁₇, and -C(=O)O-R₁₉-NR₁₆NR₁₇ in which k, R₁₆, R₁₇, and R₁₉ are as defined in the compound of formula (I), optionally, its racemic forms, isomers thereof, N-oxydes thereof, and its pharmaceutically acceptable salts thereof.~~

17- A compound according to claim 1 selected from:

- Sch 31*
- 5 - benzyl 4-benzyl-5-oxo-4H-[1,2,4]triazolo[4,3-a]quinazol-7-ylcarboxylate,
- 10 - 4-pyridylmethyl 4-benzyl-5-oxo-4H-[1,2,4]triazolo[4,3-a]quinazol-7-ylcarboxylate,
- 15 - *N*-(3,4-methylenedioxybenzyl)-4-benzyl-5-oxo-4H-[1,2,4]triazolo[4,3-a]quinazol-7-ylcarboxamide,
- 20 - *N*-(4-pyridylmethyl)-4-benzyl-5-oxo-4H-[1,2,4]triazolo[4,3-a]quinazol-7-ylcarboxamide,
- 25 - *N*-(3,4-methylenedioxybenzyl)-4-benzyl-5-oxo-4H-imidazo[1,2-a]quinazol-7-ylcarboxamide,
- 30 - *N*-(4-pyridylmethyl)-4-benzyl-5-oxo-4H-imidazo[1,2-a]quinazol-7-ylcarboxamide,
- *N*-(4-methoxybenzyl)-4-benzyl-5-oxo-4,5-dihydro[1,2,4]triazolo[4,3-a]quinazoline-7-carboxamide,
- *N*-[3-(4-pyridylsulphanyl)propyl]-4-benzyl-5-oxo-4,5-dihydro[1,2,4]triazolo-[4,3-a]quinazoline-7-carboxamide,
- *N*-(3,4-Methylenedioxybenzyl)-4-(4-cyanobenzyl)-5-oxo-4H-[1,2,4]triazolo[4,3-a]quinazol-7-ylcarboxamide
- Methyl 4-{7-[(1,3-benzodioxol-5-ylmethyl)-carbamoyl]-5-oxo-5H-[1,2,4]triazolo[4,3-a] quinazol-4-ylmethyl} benzoate
- Methyl 4-{7-[(4-methoxybenzyl)-carbamoyl]-5-oxo-5H-[1,2,4]triazolo[4,3-a] quinazol-4-ylmethyl} benzoate
- Methyl 4-{7-[(pyridin-4-ylmethyl)-carbamoyl]-5-oxo-5H-[1,2,4]triazolo[4,3-a] quinazol-4-ylmethyl} benzoate
- (2-Dimethylamino-ethyl) 4-[7-(4-fluoro-benzylcarbamoyl)-5-oxo-5H-[1,2,4]triazolo[4,3-a]quinazol-4-ylmethyl] benzoate
- 4-(4-Dimethylcarbamoyl-benzyl)-5-oxo-4,5-dihydro-[1,2,4]triazolo[4,3-a]quinazoline-7-carboxylic acid 4-methoxy-benzylamide
- *N*-(pyridin-4-ylmethyl)-4-(4-cyanobenzyl)-5-oxo-4H-[1,2,4]triazolo[4,3-a]quinazol-7-ylcarboxamide

- Suh
β*
- Methyl (4-{7-[(1,3-benzodioxol-5-ylmethyl)-carbamoyl]-5-oxo-5H-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetate
 - Methyl (4-{7-[(4-methoxy)-benzylcarbamoyl]-5-oxo-5H-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetate
 - 5 - Methyl (4-{7-[(pyridin-4-yl)-methylcarbamoyl]-5-oxo-5H-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetate
 - *N*-(pyridin-4-ylmethyl) 4-[3-(pyridin-4-yl)-2-propen-1-yl]-5-oxo-4*H*-[1,2,4]triazolo[4,3-*a*]quinazol-7-ylcarboxamide
 - 4-[2-(4-Chloro-phenoxy)-ethyl]-5-oxo-4,5-dihydro-[1,2,4]triazolo[4,3-*a*]quinazoline-7-carboxylic acid 4-methoxy-benzylamide
 - 10 - 4-{7-[(4-methoxybenzyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazol-4-ylmethyl} benzoic acid
 - 4-{7-[(1,3-benzodioxol-5-ylmethyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazol-4-ylmethyl} benzoic acid
 - 15 - 4-{7-[(pyridin-4-ylmethyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazol-4-ylmethyl} benzoic acid
 - 4-{7-[(4-fluoro)-benzylcarbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazol-4-ylmethyl} benzoic acid
 - (4-{7-[(4-methoxy)-benzylcarbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetic acid
 - 20 - (4-{7-[(1,3-benzodioxol-5-ylmethyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetic acid, and
 - (4-{7-[(pyridin-4-yl)-methylcarbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetic acid.
- 25 18- A compound according to claim 1 selected from :
- benzyl 4-benzyl-5-oxo-4*H*-[1,2,4]triazolo[4,3-*a*]quinazol-7-ylcarboxylate,
 4-pyridylmethyl 4-benzyl-5-oxo-4*H*-[1,2,4]triazolo[4,3-*a*]quinazol-7-ylcarboxylate,
N-(3,4-methylenedioxybenzyl)-4-benzyl-5-oxo-4*H*-[1,2,4]triazolo[4,3-*a*]quinazol-7-ylcarboxamide,
- 30 *N*-(4-methoxybenzyl)-4-benzyl-5-oxo-4,5-dihydro[1,2,4]triazolo[4,3-*a*]quinazoline-7-carboxamide,

N-(3,4-Methylenedioxybenzyl)-4-(4-cyanobenzyl)-5-oxo-4*H*-[1,2,4]triazolo[4,3-*a*]quinazol-7-ylcarboxamide

Methyl 4-{7-[(1,3-benzodioxol-5-ylmethyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazol-4-ylmethyl} benzoate

5 Methyl 4-{7-[(4-methoxybenzyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazol-4-ylmethyl} benzoate

4-(4-Dimethylcarbamoyl-benzyl)-5-oxo-4,5-dihydro-[1,2,4]triazolo[4,3-*a*]quinazoline-7-carboxylic acid 4-methoxy-benzylamide

Methyl (4-{7-[(1,3-benzodioxol-5-ylmethyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetate

Methyl (4-{7-[(4-methoxy)-benzylcarbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetate

4-{7-[(4-methoxybenzyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazol-4-ylmethyl} benzoic acid

15 4-{7-[(1,3-benzodioxol-5-ylmethyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazol-4-ylmethyl} benzoic acid

4-{7-[(pyridin-4-ylmethyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazol-4-ylmethyl} benzoic acid

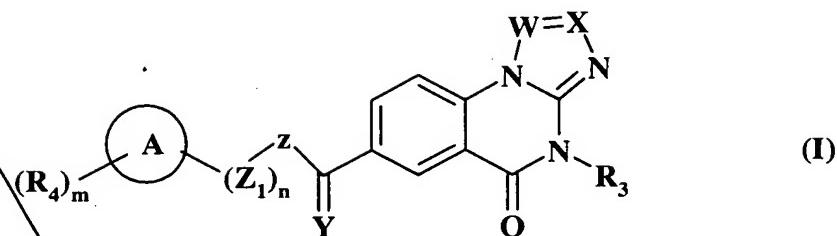
20 4-{7-[(4-fluoro)-benzylcarbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazol-4-ylmethyl} benzoic acid

(4-{7-[(4-methoxy)-benzylcarbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetic acid

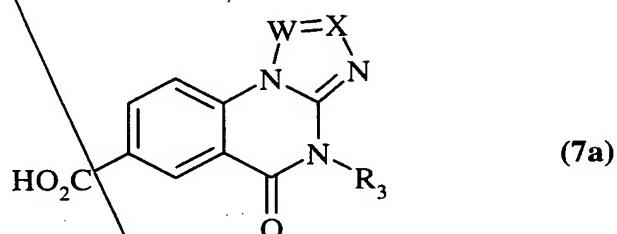
(4-{7-[(1,3-benzodioxol-5-ylmethyl)-carbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetic acid, and

25 (4-{7-[(pyridin-4-yl)-methylcarbamoyl]-5-oxo-5*H*-[1,2,4]triazolo[4,3-*a*]quinazolin-4-ylmethyl}-phenyl)-acetic acid.

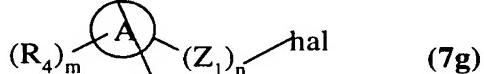
19. Process for manufacturing a compound of general formula (I)



in which W, X, R₃, R₄, n, m, Z₁ and A are as defined in claim 1, Y is O and Z is O, the said process being characterized in that it comprises the reaction of the compound of formula (7a):

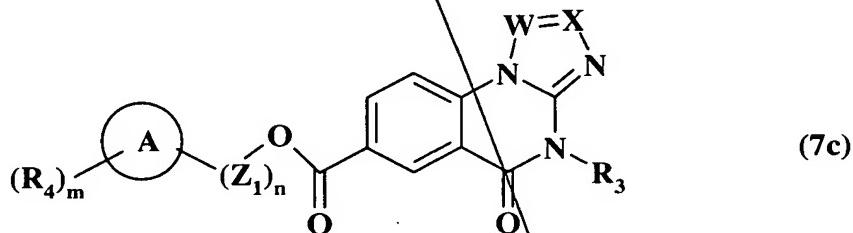


in which W, X, and R₃ are as defined in the compound of formula (I), with the compound of general formula (7g), in the presence of a base:

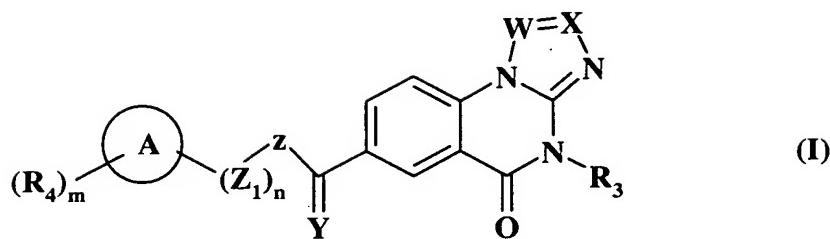


in which hal is a halogen atom, and in which R₄, n, m, Z₁ and A are as in the compound of formula (I),

to give the compound of general formula (7c), which is a particular case of the compounds of formula (I):

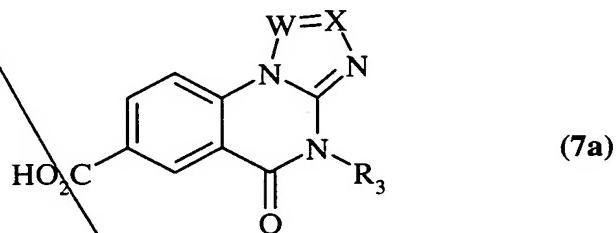


in which W, X, R₃, R₄, n, m, Z₁ and A are as defined hereinbefore.

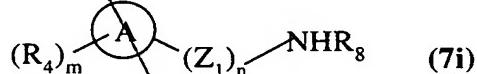


Suh
b1

in which W, X, R₃, R₄, n, m, Z₁ and A are as defined in claim 1, Y is O and Z is -NR₈, in which R₈ is as defined in claim 1, the said process being characterized in that it comprises the reaction of the compound of formula (7a):

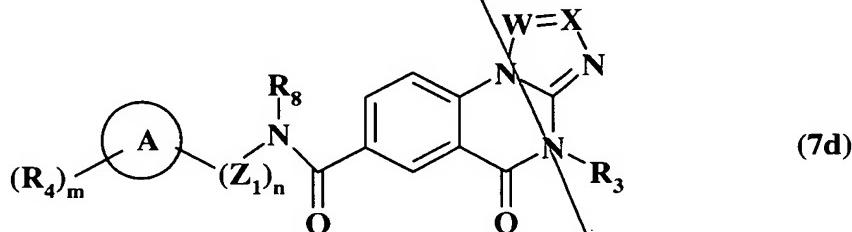


in which W, X, and R₃ are as defined in the compound of formula (I), with the compound of general formula (7i) :



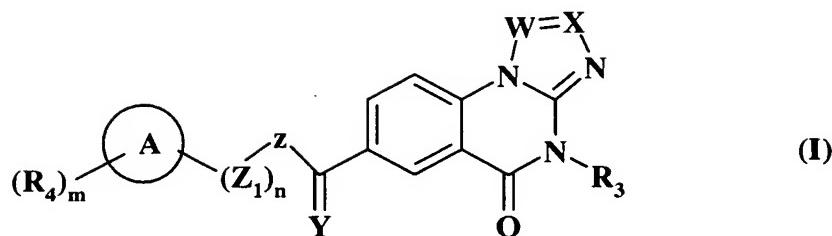
in which R₄, R₈, n, m, Z₁ and A are as defined in the compound of formula (I),

- 10 by activating the acid function with an activator, in the presence of diisopropylethylamine (DIPEA) and in a solvent, to give the compound of general formula (7d), which is a particular case of the compounds of formula (I):

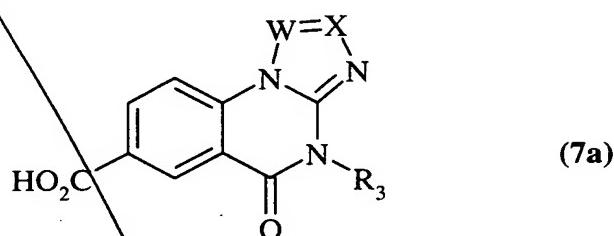


in which W, X, R₃, R₄, R₈, n, m, Z₁ and A are as defined hereinbefore.

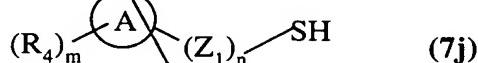
- 15 21 - Process for manufacturing a compound of general formula (I),



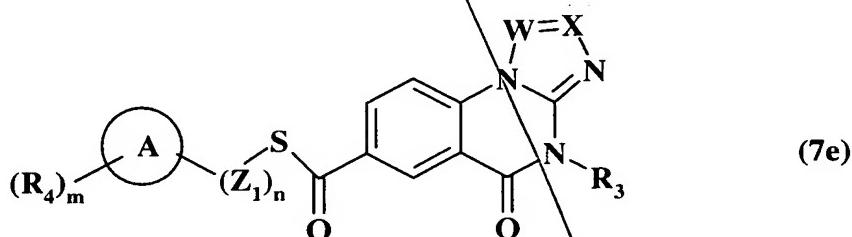
in which W, X, R₃, R₄, n, m, Z₁ and A are as defined in claim 1, Y is O and Z is S, the said process being characterized in that it comprises the reaction of the compound of formula (7a):



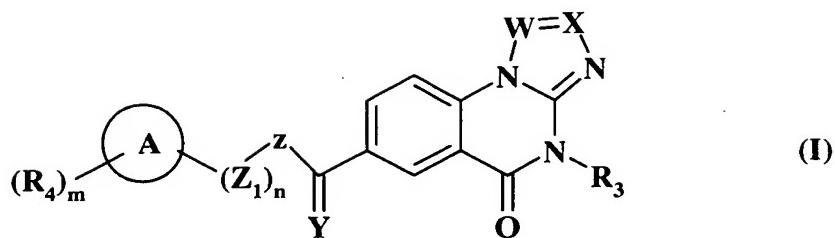
in which W, X, and R₃ are as defined in the compound of formula (I), with the compound of general formula (7j):



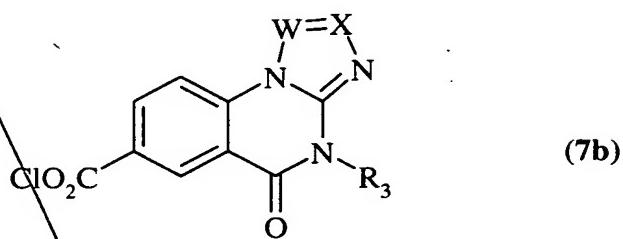
in which R₄, n, m, Z₁ and A are as defined in the compound of formula (I), by activating the acid function with an activator, in the presence of DIPEA in a solvent, to give the compound of general formula (7e), which is a particular case of the compounds of formula (I):



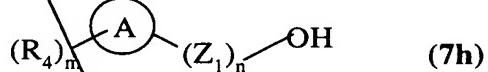
in which W, X, R₃, R₄, n, m, Z₁ and A are as defined hereinbefore.



in which W, X, R₃, R₄, n, m, Z₁ and A are as defined in claim 1, Y is O and Z is O, the said process being characterized in that it comprises the reaction of the compound of formula (7b):

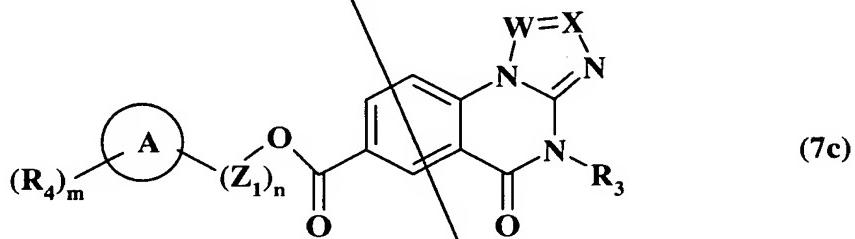


in which W, X, and R₃ are as defined in the compound of formula (I), with the compound of formula (7h):



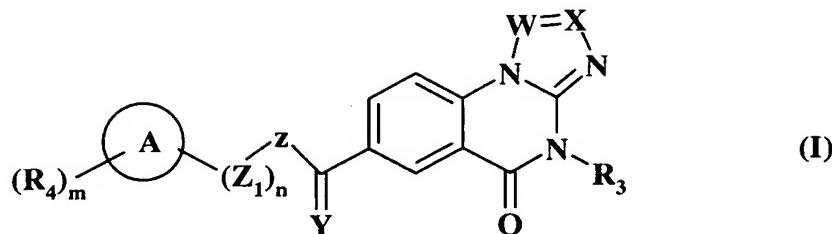
in which R₄, n, m, Z₁ and A are as defined in the compound of formula (I),

in the presence of a base, to give the compound of general formula (7c), which is a particular case of the compounds of formula (I):

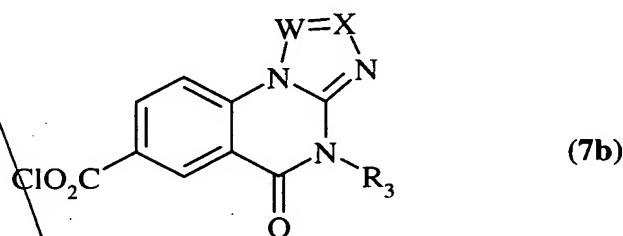


in which W, X, R₃, R₄, n, m, Z₁ and A are as defined hereinbefore.

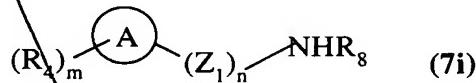
23 -. Process for manufacturing a compound of general formula (I),



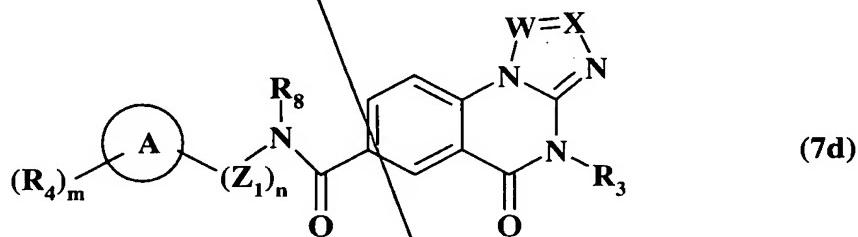
in which W, X, R₃, R₄, n, m, Z₁ and A are as defined in claim 1, Y is O and Z is -NR₈, in which R₈ is as defined in claim 1, the said process being characterized in that it comprises the reaction of the compound of formula (7b):



in which W, X, and R₃ are as defined in the compound of formula (I), with the compound of formula (7i):

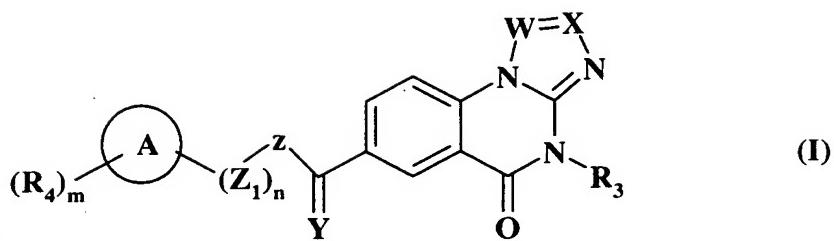


in which R₄, R₈, n, m, Z₁ and A are as defined in the compound of formula (I), in the presence of a base, to give the compound of general formula (7d), which is a particular case of the compounds of formula (I):

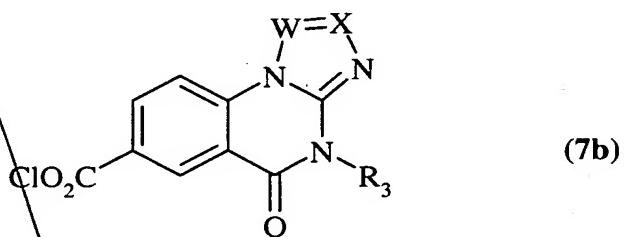


in which W, X, R₃, R₄, R₈, n, m, Z₁ and A are as defined hereinbefore.

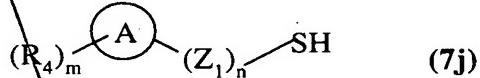
24 - . Process for manufacturing a compound of general formula (I),



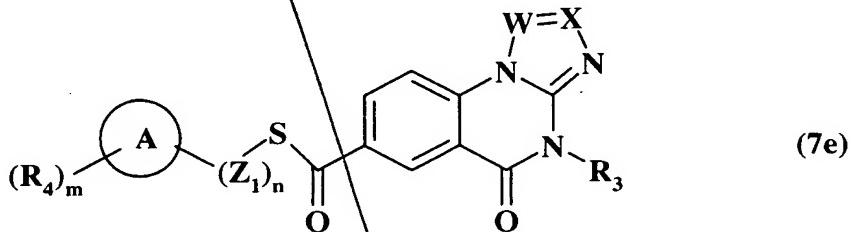
in which W, X, R₃, R₄, n, m, Z₁ and A are as defined above, Y is O and Z is S, the said process being characterized in that it comprises the reaction of the compound of formula (7b):



in which W, X, and R₃ are as defined in the compound of formula (I), with the compound of general formula (7j):

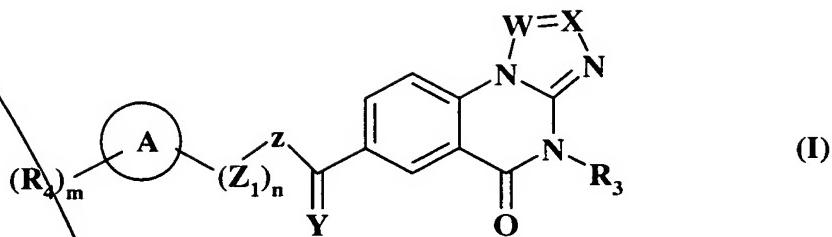


in which R₄, n, m, Z₁ and A are as defined in the compound of formula (I), to give the compound of general formula (7e), which is a particular case of the compounds of formula (I):

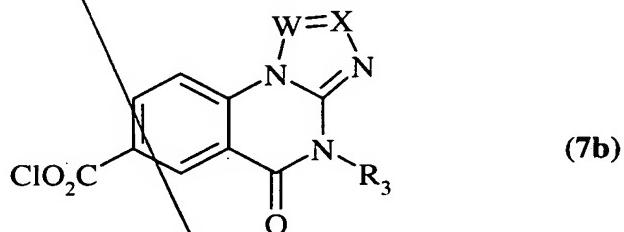


in which W, X, R₃, R₄, n, m, Z₁ and A are as defined hereinbefore.

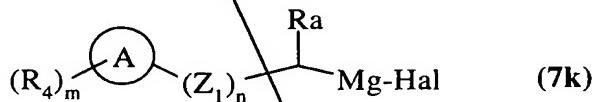
25 - . Process for manufacturing a compound of general formula (I),



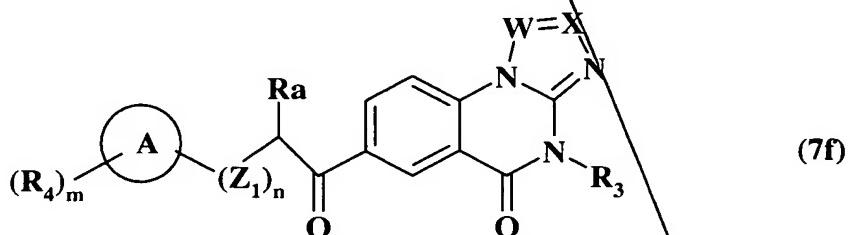
in which W, X, R₃, R₄, n, m, Z₁ and A are as defined above, Y is O and Z is -CHRa, in which Ra represents a group selected from hydrogen, (C₁-C₆)alkyl, aryl, aryl(C₁-C₆)alkyl, aromatic heterocycle, non-aromatic heterocycle, and cycloalkyl, the said process being characterized in that it comprises the reaction of the compound of formula (7b):



in which W, X, and R₃ are as defined in the compound of formula (I), with the compound of general formula (7k):

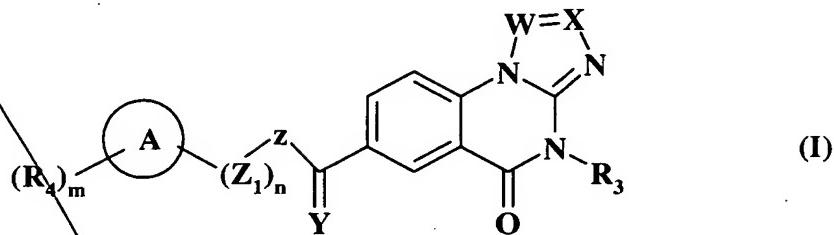


- 10 in which Ra represents a group selected from hydrogen, (C₁-C₆)alkyl, aryl, aryl(C₁-C₆)alkyl, aromatic heterocycle, non-aromatic heterocycle, and cycloalkyl, Hal represents a halogen atom, and R₄, n, m, Z₁ and A are as defined in the compound of formula (I), to give the compound of general formula (7f), which is a particular case of the compounds of formula (I):
- 15



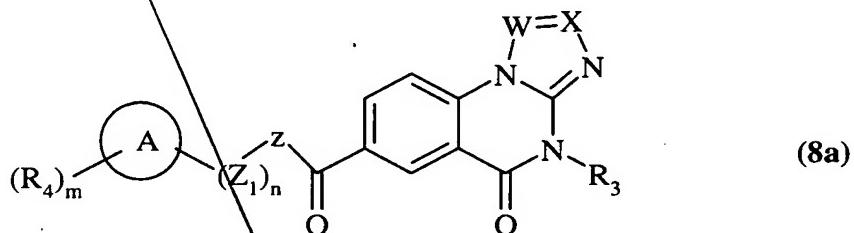
in which W, X, R₃, R₄, Ra, n, m, Z₁ and A are as defined hereinbefore.

26 -. Process for manufacturing a compound of general formula (I),

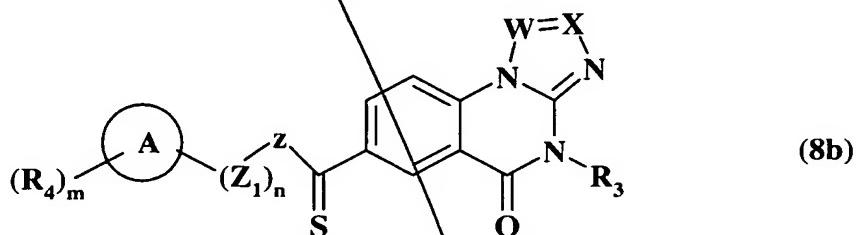


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in which W, X, R_3 , R_4 , n, m, Z, Z_1 and A are as defined in claim 1, and Y is S, the said process being characterized in that it comprises the reaction of the compound (8a):

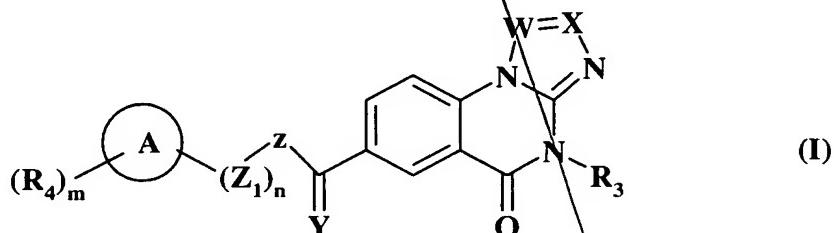


5 in which W, X, R_3 , R_4 , n, m, Z, Z_1 and A are as defined in the compound of formula (I), with Lawesson's reagent or P_2S_5 , to give the compound of general formula (8b), which is a particular case of the compounds of formula (I):

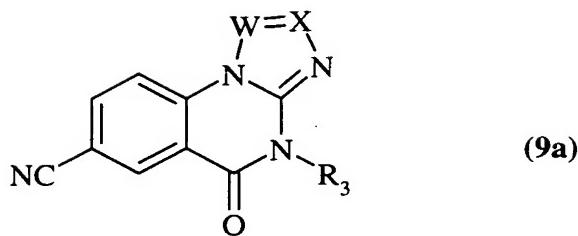


10 in which W, X, R_3 , R_4 , n, m, Z, Z_1 and A are as defined hereinbefore.

27 -. Process for manufacturing a compound of general formula (I),



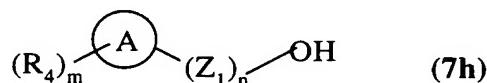
15 in which W, X, R_3 , R_4 , n, m, Z_1 and A are as defined in claim 1, Y is NH and Z is O, the said process being characterized in that it comprises the reaction of compound (9a):



(9a)

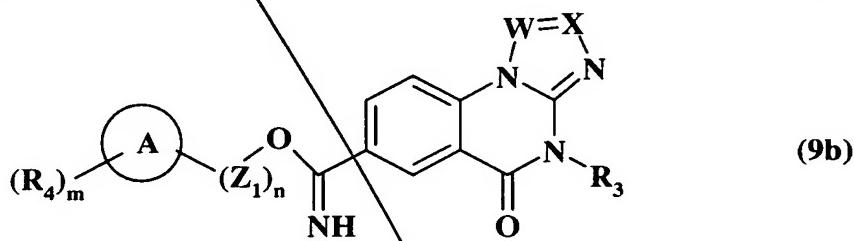
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in which W, X, and R₃ are as defined in the compound of formula (I), with the compound of general formula (7h):



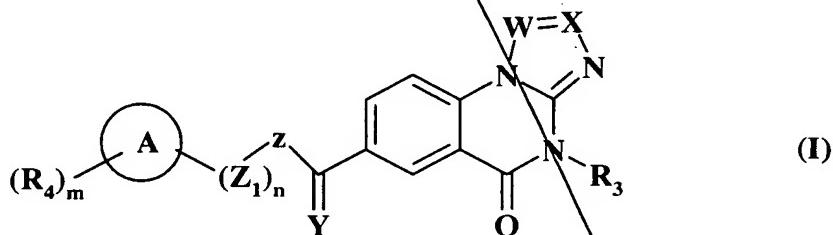
5 in which R₄, n, m, Z₁ and A are as defined in the compound of formula (I),

to give the compound of general formula (9b), which is a particular case of the compounds of formula (I):

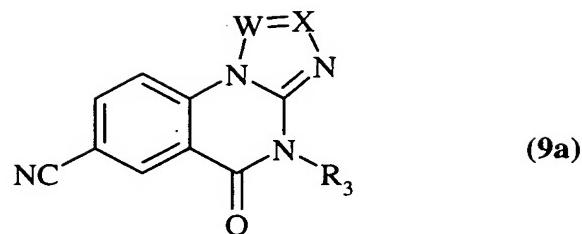


in which W, X, R₃, R₄, n, m, Z₁ and A are as defined hereinbefore.

10 28 -. Process for manufacturing a compound of general formula (I),

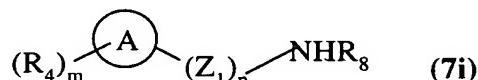


in which W, X, R₃, R₄, n, m, Z₁ and A are as defined in claim 1, Z is -NR₈ and Y is NH, the said process being characterized in that it comprises the reaction of compound (9a):

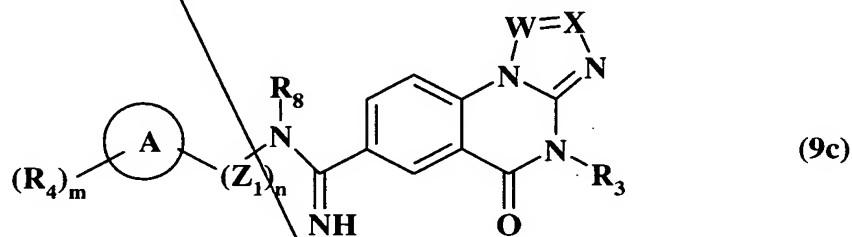


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in which W, X and R₃ are as defined in the compound of formula (I), with the compound of general formula (7i):

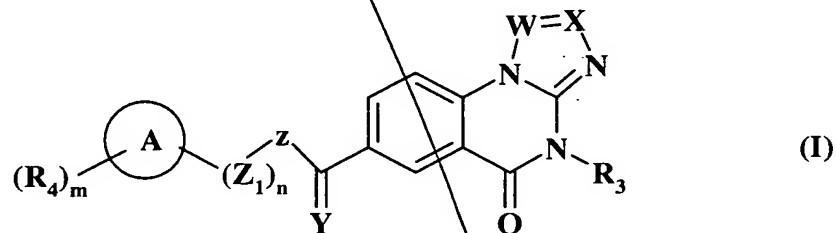


- 5 in which R₄, n, m, Z₁ and A are as defined in the compound of formula (I), to give the compound of general formula (9c), which is a particular case of the compounds of formula (I):

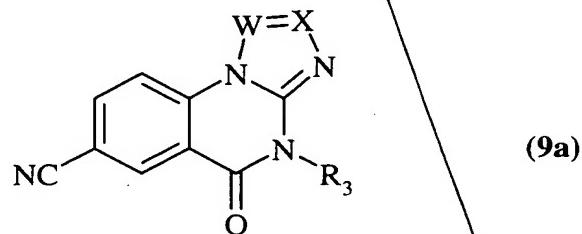


in which W, X, R₃, R₄, R₈, n, m, Z₁ and A are as defined hereinbefore.

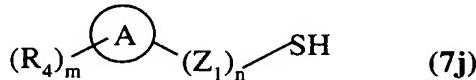
- 10 29 -. Process for manufacturing a compound of general formula (I),



in which W, X, R₃, R₄, n, m, Z₁ and A are as defined in claim 1, Z is S and Y is NH, the said process being characterized in that it comprises the reaction of compound (9a):

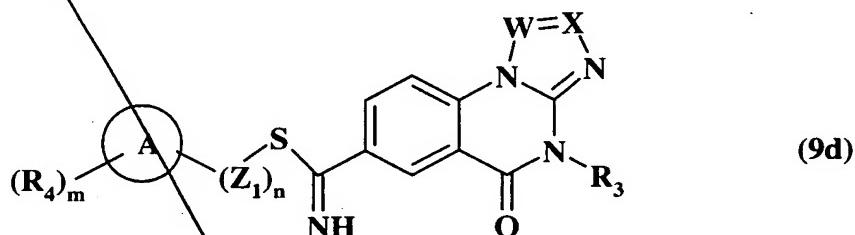


in which W, X, and R₃ are as defined in the compound of formula (I), with the compound of general formula (7j):



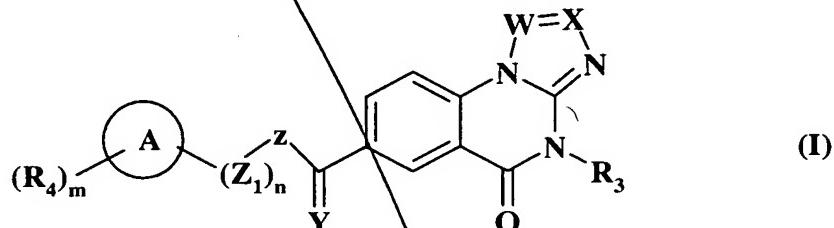
in which R₄, n, m, Z₁ and A are as defined in the compound of formula (I),

to give the compound of general formula (9d) which is a particular case of the compounds of formula (I):

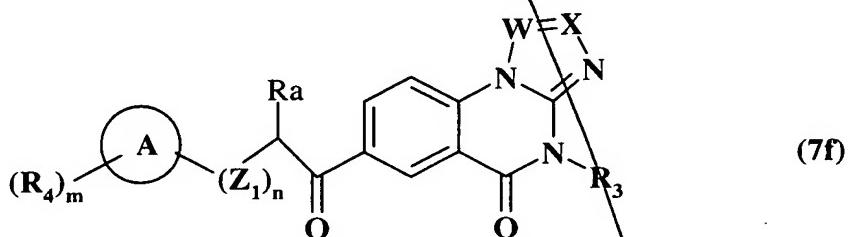


in which W, X, R₃, R₄, n, m, Z₁ and A are as defined hereinbefore.

30 -. Process for manufacturing a compound of general formula (I),

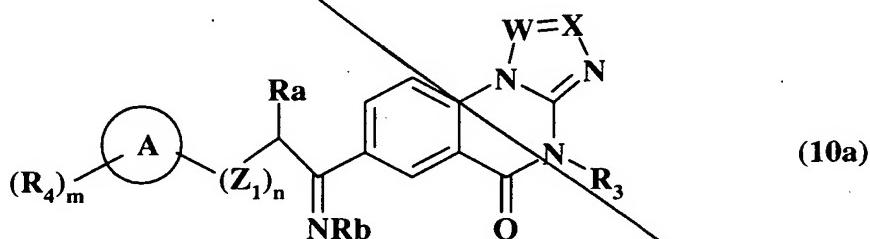


in which W, X, R₃, R₄, n, m, Z₁ and A are as defined in claim 1, Z is -CHRa in which Ra represents a group selected from hydrogen, (C₁-C₆)alkyl, aryl, aryl(C₁-C₆)alkyl, aromatic heterocycle, non-aromatic heterocycle, and cycloalkyl, and Y is N-Rb in which Rb is a (C₁-C₆)alkyl, the said process being characterized in that it comprises the reaction of compound (7f):



in which W, X, R₃, R₄, n, m, Z₁ and A are as defined in the compound of formula (I), and in which Ra is as defined hereinbefore,

with Rb-NH₂, in which Rb represents a (C₁-C₆)alkyl group, in a presence of a dehydrating agent, to give the compound of general formula (10a), which is a particular case of the compounds of formula (I):



in which W, X, R₃, R₄, n, m, Z₁, Ra, Rb and A are as defined hereinbefore.

31.- Pharmaceutical composition comprising a compound according to any one of Claims 1 to 18 and a pharmaceutically acceptable excipient.

32 -. Use of a compound according to any one of Claims 1 to 18, for the preparation of a medicinal product intended for treating a disease or complaint involving therapy by inhibition of type-13 matrix metalloprotease.

33 -. Use of a compound according to any one of Claims 1 to 18, for the preparation of a medicinal product intended for treating arthritis, rheumatoid arthritis, osteoarthritis, osteoporosis, periodontal diseases, inflammatory bowel disease, psoriasis, multiple sclerosis, cardiac insufficiency, atherosclerosis, asthma, chronic obstructive pulmonary diseases, age-related macular degeneration and cancer.

34 - Use according to Claim 33; characterized in that the disease is arthritis.

20 35 - Use according to Claim 33, characterized in that the disease is osteoarthritis.

36 -. Use according to Claim 33, characterized in that the disease is rheumatoid arthritis.

37 - A method for treating a disease or complaint involving a therapy by inhibition of MMP-13, the said method comprising the administration of an effective amount of a compound according to any one of Claims 1 to 18 to a patient.

~~38- A method for treating a disease according to Claim 37 characterized in that the disease or the complaint are selected from arthritis, rheumatoid arthritis, osteoarthritis, osteoporosis, periodontal diseases, inflammatory bowel disease, psoriasis, multiple sclerosis, cardiac insufficiency, atherosclerosis, asthma, chronic obstructive pulmonary disease (COPD), age-related macular degeneration (ARMD) and cancers.~~

39- A method for treating a disease according to Claim 37 characterized in that the disease is arthritis.

40- A method for treating a disease according to Claim 37 characterized in that the disease is osteoarthritis.

41- A method for treating a disease according to Claim 37 characterized in that the disease is rheumatoid arthritis.

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